On

N A R C O L E P S Y,

A DISEASE SUI GENERIS: WITH A SHORT ENQUIRY INTO THE NATURE OF SLEEP.

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ON NARCOLEPSY - A DISEASE SUI GENERIS: WITH A SHORT ENQUIRY INTO THE NATURE OF SLEEP.

"The great field for new discoveries is always the unclassified residuum." (W.JAMES).

INTRODUCTION.

My main thesis is that there exists in the great "unclassified residuum" on the borderline of epilepsy a highly remarkable and by no means very rare disease with peculiar and unmistakable features that distinguish it clearly from epilepsy and other morbid conditions with which it is at present confounded. The victims of this disease have sudden attacks of two kinds: in one they are overcome by an irresistible desire to sleep; in the other, which is brought on by emotion, especially by hearty laughter, the muscles relax and lose their power so that the patients sink helpless to the ground. In other respects they are perfectly healthy and earn their living in occupations demanding high intelligence or good muscular power.

The first case, so far as I am aware, was described by Westphal in 1887 in a paper on "eigenartige mit

Einschlafen verbundene Anfälle."

In 1880 Gelineau described another case and used the word Narcolepsy for the first time. This writer asserted that he had described "a new form of neurosis" that was quite distinct from epilepsy. His lucid account should have prevented his successors from using the word he had coined for cases which did not conform to his description, but unfortunately it was misapplied. The same mistake was made after Erb's description of Thomsen's disease. Just as later writers confused the symptom myotonia with the disease myotonia congenita and described various dissimilar conditions as "atypical Thomsen's disease," thus creating confusion that persisted for several decades and still finds expression in medical writings, so Gelineau's description of narcolepsy was forgotten, the new word was applied indiscriminately to any and every condition in which sleep is excessive, its value was lost and its author's valuable work completely stultified.

The following excerpts from standard text-books on medicine, neurology and psychiatry will show that the name narcolepsy is applied at present to a symptom-excessive or untimely sleep - and not to the definite disease for which Gelineau invented the word.

In the eighth edition (1919) of Osler's System of Medicine, narcolepsy appears in the index and refers to

the following words in the chapter on obesity: "A remarkable phenomenon associated with excessive fat in young persons is an uncontrollable tendency to sleep - like the fat boy in Pickwick. It is quite possible that this narcolepsy is also a manifestation of disturbed internal secretions." In later editions narcolepsy is not indexed.

In Allbutt and Rolleston's System of Medicine the Index reference to narcolepsy guides us to a paragraph in Dr. Guthrie's article on night-terrors!

In Oxford Medicine edited by Christian and Mackenzie, Dr. Saunders wrote: "Narcolepsy is a state of profound sleep into which hysterical subjects are liable to fall suddenly." But as we shall see later the sleep is rarely profound and the subjects of true narcolepsy are not hysterical.

In the Dictionary of Practical Medicine edited by Morris, Langmead and Holmes, Dr. Holmes states that "Narcolepsy is a rare neurosis characterised by a sudden and irresistible desire to sleep which recurs at intervals. The sleep which is profound may be of short duration or may last for days." Here there is no reference to the characteristic attacks on emotion. The sleep in true narcolepsy is usually very light and never lasts for days.

In the chapter on hysteria in Oppenheim's Textbook of Nervous Disease, a few lines in small print are

given to narcolepsy. There is no mention of the effect of emotion and it is said that "narcolepsy certainly occurs in other diseases, especially as an equivalent of an epileptic attack and from mental degeneration but it is often of an hysterical nature. It may occur in general obesity."

Bleuler in his Lehrbuch der Psychiatrie writing on stuperose states in Hysteria says "dann sehen wir Schlafzustände von sekunden - bis jahrelanger Dauer (Narkolepsie wenn sie den Patienten plötzlich überfallen und nicht lange anhalten; solche Anfälle können aber auch anderer z.b. epileptischer Natur sein)."

Stoddart in "Mind and its Disorders", writes: "Narcolepsy, a condition of deep sleep lasting sixteen to twenty hours sometimes occurs as an epileptic equivalent". There is no other reference to narcolepsy in the book.

As so often happens we come near the truth when we refer to Gower's "Diseases of the Nervous System". In the chapter on Trance and Catalepsy there is a paragraph on Narcolepsy where this great clinician wrote "The term 'narcolepsy' has been used in several senses but is best applied to a condition for which some name is needed in which there is a tendency to fall into sound sleep for a short time, usually a few minutes, rarely for an hour or more." He describes a case with characteristic sleep attacks but makes no mention of the effect of emotion. The

disease he says "is most likely to be confounded with minor epilepsy, but from this it is sharply distinguished by the perfect resemblance of the attacks to ordinary sleep in their onset and character."

In the text-books by Lewandowsky and Charcot-Bourchard there is no separate chapter on the disease. Dejerine says that the diagnosis narcolepsy can only be provisional as there can be "no narcolepsy without organic cause." Kraepelin considers that it is an expression of epilepsy, Bregman says that "most of the patients are hysterical, some epileptic."

Purves Stewart in the "Diagnosis of Nervous Diseases" writes, "Narcolepsy is a condition in which the patient has sudden paroxysms of apparent sleep in the midst of whatever occupation he may be pursuing at the moment. Most of these cases are hysterical. Extreme cases of hysterical narcolepsy may last for weeks, months or even years. Other cases of narcolepsy are associated with organic diseases of the pituitary body or the floor of the third ventricle. In congenital narcolepsy there occur paroxysms of sudden overwhelming sleep appearing at the age of puberty and recurring for many years afterwards. These attacks are liable to be induced by emotional excitement, particularly if the patient laughs, when his muscles suddenly relax and he falls sound asleep." Although incorrect in almost every detail, it is obvious

that this description of "congenital narcolepsy" refers to the true narcolepsy of Gelineau.

I have searched through a great number of books in which one might expect to find some reference to the disease, without finding any adequate account of it or any attempt to distinguish between true narcolepsy and symptomatic sleepiness.

As a curiosity I quote from Jelliffe and White's "Diseases of the Nervous System". In the chapter on convulsive states under the heading narcolepsy it is stated that "sudden attacks of sleepiness are usually psychogenic in origin and will often be found to disguise autoerotic phantasying and to be compulsive in charatcer."

The same confusion exists in medical journals. French writers describe narcolepsy in obesity, pituitary disease, cerebral tumour, epilepsy, hysteria and other conditions entirely ignoring the "chute ou astasie" on emotion which is always absent in diseases where sleepiness is an occasional symptom.

In Germany great confusion has existed among medical writers since Friedmann first described the "kurze narcoleptische Anfälle" which we now call pyknolepsy - short attacks quite unlike normal sleep and quite distinct from Gelineau's disease. Again and again I found that articles in German journals, with "narcolepsy" in the title, dealt with Friedmann's disease or with cases of cerebral or general disease in which sleepiness was a

symptom. So far as I know nothing has been written in English on true narcolepsy. Wherever I found the word in English writings it was used for profound somnolence or attacks of sleep as a symptom of some other disease. This evidence shows that the word narcolepsy is used at present for a symptom and not exclusively for the disease to which Gelineau applied it.

One of my objects in this thesis is to rescue the word narcolepsy from the confusion that now surrounds it and to reinstate it as the name of an important and distinct disease. I have said that the disease is by no means very rare. I say this becuase I have encountered six cases during the last year in the course of routine hospital and private work. I have said that narcolepsy is at present confounded with epilepsy because two of my cases had been diagnosed by highly competent neurological colleagues as "typical petit mal" and another by a consulting physician as "epilepsy without convulsions"; further because Kraepelin, and other authorities, consider that narcolepsy is an expression of epilepsy and Bregman states that "some of the cases are epileptic, some hysterical." I hope to show that Gelineau described a disease sui generis easily recognised and easily distinguishable from all other diseases in which sudden attacks of excessive sleep are symptoms.

I shall base my conclusions upon an analysis of five

cases that have come under my own observation and fifteen cases recorded in journals in the Library of the Royal Society of Medicine. These fifteen cases are the booty from a long search through a number of papers dealing with patients in whom "narcolepsy" was a symptom. In this search I found references to other cases which I could not trace and since I began this study several new cases have been described in German journals of neurology. I have not, therefore, included all the published cases here but those I have chosen as examples of true narcolepsy will suffice, I think, to prove that the peculiar combination of symptoms in this disease recurs with a frequency and uniformity that justify its description as a distinct disease. In these matters, "the right question is" as the late Sir Clifford Allbutt wrote "have I noted in a moving equilibrium, say in Man, that a certain series of changes, static and dynamic, has occurred more than once? If so, was the recurrence still fortuitous, or was the series a case of an orderly recurrent mode, which hitherto had escaped attention? If so, the recurrence will be observed again and again by myself or by others in approximate uniformity. The cases of the newly observed series will vary, some indeed so far as to trespass upon other nosological series already recognised, and no strict demarcation can be drawn around them; yet there may, nevertheless, be difference enough and constancy enough to make it worth our while, for the convenience of ob-

servation and thought, to erect the new series into a category of its own, and to stick a label on it?"

In the case of narcolepsy the answer to this question must be yes. The "new series" is worthy of a label because, for one reason, it comprises cases that are at present confused with the "orderly recurrent mode" that we call epilepsy, and it is certainly convenient "for observation and thought" and highly important for our patients that we should distinguish it from a serious disease with which it has no connection whatsoever.

After describing the cases briefly I shall analyse them and consider the differences between narcolepsy and certain other diseases. I shall then discuss the symptoms and attempt to explain their nature. This will entail a short inquiry into the mechanism of normal sleep and a brief review of Pavlov's researches on internal inhibition and sleep. I shall attempt to prove that the two "kinds" of attack in narcolepsy are essentially the same and not different in kind as has hitherto been thought. Further I hope to support Pavlov's conception that "internal inhibition and sleep are one and the same process" - a conception based upon the results of experiments on dogs - with evidence gained from the study of narcolepsy - a disease of man.

Finally I shall attempt to reconcile prevailing notions of the mechanism of sleep, based on the assumption

of "sleep centres" in the basal ganglia with Pavlov's work which seems to me to prove that normal sleep is a function of the cerebral cortex.

DESCRIPTION OF CASES.

Case 1. Olive P. aged 13½ came to the National Hospital, Queen Square, as an out-patient in September 1923. Her complaint according to the notes was that "she has attacks in which she comes over faint and falls (? transient loss of consciousness)". A diagnosis of petit mal was made and bromide and luminal were ordered. This had no effect upon the attacks. I saw her for the first time in May 1924 and have seen her at regular intervals since. At her first visit I wrote down her own words: "When I laugh I cannot stand. I must sit down in a chair or I will fall." Thinking her case was one of Lachschlag (Oppenheim) I looked up this subject and so came across Gelineau's narcolepsy. At her next visit I questioned her more closely and obtained the following information. She suffers from two distinct kinds of attacks, first attacks in which she falls asleep and secondly attacks of weakness in the limbs on laughing. She has always been a heavy sleeper and is always rather sleepy during the day. During her twelfth year she began to fall asleep during the day. In her mother's words "after doing a little work in the house she is played out

and goes off into a sound sleep." These attacks now occur several times every day. When she feels the inclination to sleep she must sleep however much she tries to prevent it. She seems to be in a natural sleep and is easily awakened; she knows she has slept but has no knowledge of what has happened while she was asleep. She has fallen asleep walking in crowded streets and at other inconvenient times. The other attacks are always brought on by laughing. "If anybody makes me laugh I feel as if I shall fall down." "If anyone tells me a joke and I see it very much, my eyes go misty, I feel funny in the head, and if I don't sit down I fall down." In the attack "she opens her mouth, her head falls forward, the arms fall to her side and the knees give way." I have questioned the patient and her mother very closely on many occasions but have never obtained an account of anything resembling an epileptic attack. The family history is good. No member as far as is known has suffered from epilepsy or any mental disease. She has six brothers and sisters all healthy. Her previous health has been remarkably good; apart from measles and chickenpox she has never suffered from any illness; she did well at school. She is a pretty, well developed, healthy looking child; the menses began at the age of 13; they are not yet regular; a careful physical examination reveals no evidence of disease. She is quiet in her manner and rather shy, but on longer

acquaintance she became less reticent and discussed her symptoms freely; her intelligence is normal and she is well informed for her age. I have conversed with her and her mother on about twenty occasions and have formed the impression that apart from the attacks she is a perfectly normal girl physically and mentally.

The sleep attacks have not altered in frequency during the year that she has attended the Hospital. She has now learned to check herself when she feels inclined to laugh and the falling attacks are therefore not so frequent as before. She has never fallen asleep after laughing. I have not seen her in a sleeping attack and I was unable to provoke an attack on laughing.

Case 2. Captain X. R.A.M.C.. This officer spoke to me after a lecture and apologised for falling asleep, saying that it was impossible for him to keep awake when his attacks came on. He is now 35 and has had the attacks since the age of 20. He sleeps many times every day under all conceivable circumstances. On one occasion he fell asleep while driving his car. I sat near him on a guest night at his Corps Mess and noticed that he fell asleep twice during dinner. He served throughout the War but noise, danger and excitement did not prevent the attacks. If he laughs heartily he goes "floppy all over" and must support himself or sit down. He comes of a healthy

family and is himself perfectly healthy in every other respect. It did not occur to him that he was suffering from any definite disease and he has never sought medical advice for his troubles although his comrades never allow him to forget that he is different from normal individuals.

Case 3. Mrs. C. aged 42, consulted me because a "young doctor" told her she had cancer of the breast. The breast was healthy but in the course of conversation she described curious attacks from which she had suffered for several years. The first attack occurred when she heard that a boy who was cycling from London to spend a weekend at her house had been killed on the way. On hearing this news "all the power went from her" and she sank upon a couch where she lay powerless, unable to move and unable to say a word. Since then she has had many attacks, almost always associated with some unpleasant emotion. These attacks cause her great distress, and she now has a morbid fear that she will be found in an attack and looked upon as dead. Her eyes close at the onset of the attack and she is forced to lie down; she tries to cry for help but no sound is emitted and she makes no movement. She hears and understands everything that goes on around her and is greatly distressed because she cannot answer sympathetic enquiries. She has never fallen asleep after

one of these attacks but she has always been a "sleepy-head" and has often dropped off to sleep at inappropriate times. She consulted several physicians who diagnosed hysteria; a London consultant said she had "epilepsy without convulsions" and ordered anti-epileptic remedies. Her physical condition is good and there is nothing in her personal or family history to account for the attacks. I was able to reassure her on two points: she would not be buried alive and she was not an epileptic.

Case 4. Leslie W. Aged 16, messenger, has suffered for the last year from sudden attacks in which he falls asleep. He had chickenpox and measles in childhood, otherwise his health has been perfect. His father and mother, four sisters and two brothers are alive and well; one sister used to walk in her sleep. He did well at school and worked efficiently as a messenger in a city office.

The first attack of sleep came on after a hard day at the office when he sat down in an armchair after supper to read: he tried hard to keep awake but was unable to do so. Next day he fell asleep in his chair at the office while waiting for orders. Since then he has had several attacks every day under the most diverse conditions, e.g. while eating his dinner or while talking to friends. He does not sleep while he is moving about actively, but now whenever he is at rest, especially if he sits down, the desire

to sleep comes on. At first he has a feeling of intense drowsiness, then his head falls forward, the arms hang limply at his side, the lids droop and he is unable to remain awake, try as he will. In many of the attacks, although people around him think he is sound asleep, he knows what is going on and can repeat conversations that took place during the attack. He wakens easily if anyone touches him or calls to him sharply but he cannot rouse himself. If left alone he sleeps for several minutes; if he happens to be in a comfortable position he sleeps for fifteen or thirty minutes. Between the attacks he feels quite well. He sleeps soundly throughout the night and finds it hard to wake up in the morning.

Whilst in Hospital several attacks were observed. In one he fell asleep while talking to the matron. He knew what she was saying and tried to answer her but could not do so; then his head dropped, his eyes closed and he slept standing up for a few seconds. On another occasion he was overcome while helping a patient to dress; he sat down and slept for two or three minutes.

In this case there were no tone-loss attacks on emotion. Physical examination revealed no abnormality. Good memory, intelligent, alert. Blood and cerebro-spinal fluid normal; pituitary fossa normal on X-ray examination. The attacks became less frequent while resting in hospital but after his discharge they returned with the previous frequency.

Case 5. Freda W. aged 17, complained of falling asleep at work and when walking about, and of falling down when she laughed. These attacks began six years ago. She had measles, whooping cough and mumps in childhood; her periods began at the age of fifteen; during her seventeenth year they were irregular, but they are now normal. The father, mother, brother and sister are all alive and well; one brother was killed in action. There is no history of nervous or mental troubles in the family.

During the summer of 1918 when she was 14 years old she began to sleep at odd times during the day, at meals, working in the house, walking in the street and when riding a bicycle. On one occasion she fell into the fire and burnt her wrists; on another she fell from her bicycle and slept in the middle of the road. She is quite unable to resist sleep; she feels drowsy, her head feels "as if the brain wants to expand" and in a few moments she is asleep. She wakes easily if touched or called and then feels as if she had been asleep in a stuffy room. Under observation in Hospital she had about ten attacks of sleep each day. Her appearance during the attack was that of a person in normal quiet sleep.

About a year after the sleepiness appeared she noticed that if she laughed heartily the "limbs crumpled up" and she fell down. Such an attack very often ended in a short sleep. At first she always slept for a time after falling down through laughing, but now these attacks are

sometimes slighter so that although she falls she remains quite conscious of her surroundings. One of these attacks was observed while she was in hospital; after laughing the lips and eyelids trembled, the head fell, she lay back on the pillow and slept for about thirty seconds.

A complete physical examination revealed nothing abnormal except that the pituitary fossa was small. Memory and intelligence were normal. She slept well at night. The attacks became much less frequent while she was resting in hospital, but she reports by letter that they became much more frequent again when she returned to her work as a domestic servant.

CASES OBSERVED BY OTHERS.

Case 6. Gelineau. A cooper aged 38; good family and personal history. For two years has had attacks in which he suddenly loses the use of his legs which suddenly give way beneath him. These attacks come on when he laughs heartily or has any pleasurable emotion such as the prospect of a good business deal, or when he holds a good hand at cards. He is worried at all times by an inclination to sleep and the attacks of weakness on emotion often end in his falling asleep for a few moments.

During a meal he may fall asleep four or five times; his knife and fork fall, the sentence which he had begun

in a loud voice ends feebly, the head sinks and he sleeps for a few seconds or minutes. He tries to prevent this by rubbing his eyes but his hand falls powerless. The only way to waken him is to shake him violently. On waking his head is clear and he feels quite fresh. He has innumerable attacks in the course of a day. In other respects he is perfectly healthy; his memory and intelligence are intact.

Gelineau distinguished clearly the two kinds of attack - simple sleep and the "chute ou astasie" on emotion; he denied that his patients suffered from epilepsy and stated that he had described "a new species of neurosis".

Case 7. Loewenfeld. Male aged 17½; diphtheria aged 6, no other illnesses; parents and four brothers and sisters healthy; an aunt paranoiac. He was one of the best scholars in his class throughout his school life but since the age of 13½ progress was impeded by attacks in which he went to asleep. At first they occurred in the afternoons only, but now they come on at any time, sometimes with only 10 or 15 minutes interval. At first they lasted for a few seconds only but now they last several minutes or longer. He passed through the Realschule and now works regularly in a factory. He gets no warning of the attack; it may come on under any circumstances, e.g.

at meals, at work or when walking home after his work; he wakes up when he strikes some object or a passer-by or when he steps off the kerb; he is in full possession of his senses at once.

On examination he appeared to be in perfect physical and mental health. The attacks which were observed resembled normal sleep. When he laughs his muscles relax objects fall from his hands, his jaw falls and he is unable to close his mouth.

Case 8. Stiefler. Male aged 31; Bell's palsy at the age of 18, otherwise always healthy: drank alcohol to excess between the ages of 18 and 26, teetotal since. His father, mother and three brothers were all alcoholic; apart from this the family history is good. He has one healthy child; none dead.

He did well at school but was often reproved for inattention because he fell off to sleep. Later he was discharged several times by various employers for the same reason.

He now has attacks in which he falls off to sleep, about four or five every day, lasting several minutes as a rule but sometimes longer when the circumstances are favourable. He once slept from midday on Sunday well into the night. The attacks are preceded by a feeling of intense fatigue, and sleep cannot be prevented. They are

more likely to come on during vigorous exercise than at other times. He has had them in the most diverse circumstances, even when standing or walking in busy streets. He bears two scars on his forehead caused by bumping into lamp posts. On waking he feels quite fresh, knows he has slept and can sometimes remember dreams. In the intervals he has a constant slight feeling of sleepiness and fatigue. His night sleep is sound and prolonged.

On examination his physical and mental condition apart from the attacks was normal. Several attacks were observed. His condition in the attack was exactly that seen in normal light sleep. He could be roused at once by a call or a shake. Laughter was not accompanied by anything unusual, but anger or annoyance caused a sudden feeling of helplessness, his legs gave way beneath him, and he was unable to utter a word. He retained full consciousness during these attacks.

Case 9. Henneberg. Male aged 26; father has tabes, a brother disseminated sclerosis; eneuresis till age of 6; rheumatic fever aged 6, chorea aged 8 and 13, works as a cooper; is a gymnast and cyclist.

For five years has fallen asleep five or six times a day for about fifteen minutes; the attack begins with a feeling of overwhelming fatigue, the lids feel heavy, and although he can sometimes resist the inclination to sleep

for half an hour or so, it is inevitable. He sleeps when playing cards, eating, smoking, reading and when riding his bicycle; he very seldom falls because he has time to get off his bicycle and lean against a wall. He once fell asleep at a listening post in the trenches although his tour of duty lasted half an hour only and he was well aware of the penalty. He is easily wakened and feels fresh at once: between the attacks he feels well and is not tired or sleepy.

If he laughs heartily his head falls forward, the jaw falls and the knees give way: he does not fall and is fully conscious during the attack. Anger rarely causes these attacks, but on one occasion when about to chastise his child his arm fell powerless to his side and his knees gave way beneath him. Examination revealed no mental or physical disease.

Case 10. Singer. Male aged 33; good family history; previous health good; for fifteen years has fallen asleep two or three times a day for about fifteen minutes;, attacks said to have followed a fall on the head, but the fall may have been caused by an attack. Aura of excessive fatigue: \ can sometimes resist for a time, but if successful he sleeps longer in the end. The attacks may come on at any time, during meals, in the ranks, on the march, at his post in the trenches, singing

in church, dancing with his wife, during coitus, riding a bicycle, on horseback, or ploughing. He is easily wakened, remembers the attack and aura and feels fresh at once. If he laughs heartily or is annoyed he grimaces and his knees give way but he does not fall.

Case 11. Noack. Male aged 33; good family history, no other illnesses. Has had attacks for six years, about six a day, lasting five to forty minutes. He once slept from Saturday night till Monday morning. He can ward off an attack for a time by walking briskly but always sleeps in the end; they come on when he is sitting in vehicles, at meals, at work, when smoking or when walking in the street. He is slightly feeble-minded and always feels tired and sleepy. When he laughs or is angry his head falls to one side as if loose, the arms hang loosely, he drops things from his hands and the legs give way.

Case 12. Redlich. Male aged 19; no serious illnesses; father alcoholic, family history otherwise good; did moderately well at school. For six months has had two or three attacks a day in which he falls asleep for five or ten minutes; if he lies down he sleeps longer; he once slept for 12 hours. He can resist the desire to sleep for some time but cannot prevent it altogether and the more he resists the longer he sleeps

The attacks generally come on at 10 a.m., during

the midday rest and at 4 p.m. In the intervals he is tired and sleepy and yawns frequently. He is easily wakened. For four months he has noticed that if he laughs heartily he has a feeling that he is going to fall, the knees give way and he lets things fall from his hands. He is perfectly healthy in every other respect.

Case 13. Mendel. Male aged 26; good family history; nose bleeding almost daily from the age of 8 to 22, none since. Always feels tired and sleepy; for four years he has fallen off to sleep several times a day for about 15 minutes; he is most likely to go off in a warm room, in dull weather or after the midday meal; he has slept in the middle of an interesting conversation, whilst reading a newspaper, during meals, during a heavy bombardment and on the march. He once fell asleep on listening-post duty in the trenches and narrowly avoided the penalty for this offence. He can laugh heartily with inpunity but if he feels angry his knees give way, his head falls forward, and he feels quite helpless. Healthy in other respects.

Case 14. Goldflam. Male aged 56: good family history, no serious illnesses, for 21 years has had attacks lasting a few seconds to minutes, dozens of times a day. He knows what is going on round him during the attack and often leans against something until it is over. He always

feels sleepy and tired but undertakes long business tours. About the same time as the sleeping attacks began, on raising his arm to strike his child he felt limp all over. Since then all sorts of emotional disturbances have caused similar attacks mainly affecting the legs so that he sinks helpless to the ground. This condition remained much the same during the 21 years he was under observation.

Case 15. Stöcker. Male aged 15; no serious illnesses; good family history; was always the best scholar in his class in the village school. For six months has had three or four attacks of sleep a day lasting ten to thirty minutes; feels tired then very sleepy; at work he can sometimes delay sleep until he has finished a particular task but he must sleep sooner or later; he has slept sitting and standing, in vehicles when he passes his destination, at meals when he drops his knife and fork, and walking in the street when he wakes on bumping into something. He is easily wakened by a call and is wide awake at once. His night sleep in normal. Physically and mentally he appears to be in perfect health. In the attacks he appeared to be sleeping normally.

If he is suddenly called upon to do a difficult piece of work he has a feeling of weakness all over him; when larking with his mates his strength suddenly goes and the weakest can do what he will with him.

Case 16. Somer. Male, (age at the time of observation, family and personal history and duration of symptoms not given).

Falls asleep "frequently" under all circumstances; especially after meals; hears what is going on around him, tries to speak but makes irrelevant remarks - this annoys him and wakens him; sleeps walking on the road and is wakened by striking something or stumbling. Had several attacks while under observation with every appearance of normal sleep from which he was easily awakened by shaking. Also has attacks on emotion, e.g. when laughing heartily, when about to strike his child, or whilst considering a difficult stroke at billiards. In these attacks the head falls, the lids droop, the limbs relax, he sinks slowly to the ground and is unable to move for half a minute. He remembers these attacks and everything that he hears during them.

Case 17. Jolly. Male aged 36; good family history; frequent nose-bleeding; rather backward at school; drank heavily for a few years; no serious illnesses. Six years ago after a period of great exertion with little sleep he began to fall asleep and had to be taken away from machinery; he usually sleeps if he sits down for more than a few minutes, especially if the weather is warm; he sometimes sleeps when walking in the street, and once was nearly

struck by a passing tramcar. If he laughs heartily or feels any strong emotion, the head falls forward, the jaw drops, the knees give way and he sinks to the ground unable to move for a minute or so; he is wide awake during these attacks. Otherwise healthy.

Case 18. Somer. Male aged 20; good family history, no serious illnesses; blow on head aged 8, not severe. Duration of symptoms not given; admitted for sudden attacks of weakness which caused him to sink slowly to the ground quite conscious but unable to move for a minute or so; these attacks are brought on by hearty laughter and other emotional disturbances. An attack was observed while he was dressing; his head sank, his knees gave way, he slipped down and remained sitting for half a minute; when ordered to speak he stammered, then opened his eyes slowly, spoke clearly, stood up and finished dressing himself. In some attacks he was able to repeat what was said to him; he remembers everything that happens during the attack. One day he was found fast asleep; he stated that he often fell asleep in the day-time. Physical and psychlogical examination revealed nothing abnormal.

Case 19. Goldflam. Male aged 33; good family history, no serious illnesses; at age of 19 began to fall asleep several times a day (duration of attack not

given) especially if he sits down at rest for more than 15 minutes but also when standing, walking and teaching in class; in an attack he appears to be in normal sleep; he sees everything as through a fog and hears everything as through a wall. He is easily wakened when he feels fresh at once. In this case there is no mention of attacks on emotion but I have accepted it as one of true narcolepsy because of the long duration without the appearance of any other disease in which attacks of sleep occur as a symptom.

Case 20. Goldflam. Male aged 48; good family history, no other illnesses, always a heavy sleeper. For nine years has had innumerable attacks of falling asleep in all circumstances, lasting a few seconds; he knows what is going on and supports himself e.g. against a wall until the attack is over; doing strenuous work as a merchant. The first attack occurred immediately after a blow on the head with an umbrella (? emotional factor). Here again there is no mention of attacks on emotion, but the long duration of attacks of typical sleep appears to justify the inclusion of this case under the heading of narcolepsy.

Analysis of Cases.

Sex. Of the cases I have included here 18 ~~were~~ are males, and only two, my own cases, ~~were~~ are females.

Age at Onset. The age of the patient at the onset of the disease in the published cases where the information is given was as follows:-

Stiefler	at school.
Loewenthal	13½ yrs.
Stöcker	14½ yrs.
Redlich	18 yrs.
Singer	18 yrs.
Goldflam	19 yrs.
Henneberg	21 yrs.
Noack	27 yrs.
Jolly	30 yrs.
Goldflam	35 yrs.
Goldflam	39 yrs.

Family and Personal History.

As a rule there is nothing in the family history of these patients to indicate that they belong to a neuropathic or degenerate stock. An aunt of Loewenthal's patient was a paranoiac; the father of Henneberg's patient had tabes dorsalis; the father of Redlich's patient was an alcoholic; but in almost every case where careful enquiries were made it is stated definitely that there was no evidence that heredity is an important ætiological factor. Nor does anything in the personal history recur with sufficient frequency to justify its recognition as an exciting or contributory cause. A blow on the head is mentioned in Singer's and Goldflam's cases, but in the

first it is probable that the fall was the result of the disease, and in the latter the blow was given by an umbrella.

Excessive nose-bleeding in childhood is noted in cases recorded by Mendel and Jolly.

I have made careful enquiries into the family and personal histories of my own cases. In each instance the stock was sound and the patient's previous health was remarkably good.

General Condition.

Apart from the attacks the general mental and physical condition of the patient was normal in almost every case. Noack's patient was "slightly feeble-minded" otherwise there was no defect of intelligence or peculiarity of temperament. In several cases a full psychological or psychoanalytical investigation was made with negative results. The patients had worked with success as mechanics, schoolmasters, merchants, commercial travellers, and in other occupations demanding considerable intelligence. Careful physical examinations, particularly of the nervous and endocrine systems were made in almost every case.

Redlich reports that the sella turcica was "remarkably small" in two of his unpublished cases. Jolly and Kahler made the same observation. In three cases the genitals

were small. In nine cases where a complete blood count was made, the lymphocytes were over 40% in four cases, over 30% in two, normal in two and low in one. The thyroid gland was slightly enlarged in several cases. The findings in cases examined by Aberhalden's method were inconsistent. Routine examinations of the blood and cerebrospinal fluid were always negative. In my own cases the general health was excellent. In one the sella turcica was small; but there are no other signs of pituitary disease. In Mrs. C. aged 42, the menstrual functions are still normal. In Olive P. now aged 13½, the periods are irregular, otherwise there is nothing to suggest ductless gland disease. In every case it is definitely stated that all indications of epilepsy and hysteria were completely absent.

The occurrence of sleep during the day caused attention to be directed to the amount and quality of the night sleep. Most of the patients slept well, some excessively. In none was the loss of night sleep an adequate explanation for sleeping during the day.

The attacks.

In true narcolepsy two "kinds" of sudden attack occur; the patient falls suddenly into normal sleep or, usually as a result of some emotional disturbance, the muscles suddenly become flaccid and powerless. For the sake of

brevity I shall refer to these attacks as "sleep attacks" and "tone loss attacks". The terms "kataleptische Starre" (Löwenfeld), "kataplektische Hemmung" (Henneberg), "plötzliche Tonusverlust, affektiver Tonusverlust" (Redlich), "Tonusblockade" (Stern) and "chute ou astasie" (Gelineau), have been used for the tone-loss attacks. I have thought of several short names for them, e.g. atonic attacks, but I think the name I have chosen is the best.

Sleep attacks nearly always precede tone-loss attacks but in cases described by Goldflam, Henneberg and Somer tone-loss came first.

Sleep attacks.

These vary greatly in frequency and duration in different patients but in the same patient they are fairly constant. Particulars so far as they are available are given in the following table:

Author.	Daily frequency.	Duration.
Löwenfeld	Every ten minutes	A few seconds.
Redlich	Two or three	5 to 10 minutes.
Noack	Six	5 to 40 minutes.
Goldflam	Several	No note.
Goldflam	Innumerable	A few seconds.
Goldflam	Innumerable	Seconds to minutes.
Stiefler	Three or four	A few minutes.
Stöcker	Four or five	10 to 30 minutes
Mendel	Two	Fifteen
Jolly	"Whenever he sits down to rest".	(No note).
Henneberg	Five or six	Fifteen minutes.
Singer	Two or three	A few seconds to 15 minutes.

In several cases it is stated that the patient sometimes sleeps longer when the circumstances are favourable. Noack's patient once slept for 36 hours, Redlich's for 12.

Circumstances in which sleep attacks occur.

The attacks often occur in circumstances conducive to sleep, e.g. after a meal, during the midday rest, in warm weather or in a close room, but in every patient some have occurred under conditions by no means favourable for sleep, e.g. in the midst of an interesting conversation, during a game of cards, while walking in a busy street, while ploughing, riding or cycling, on the march, during bombardments, on listening-post duty where the penalty for sleeping is death, in fact in all conceivable circumstances. My friend the R.A.M.C. officer once went to sleep while driving his car and woke to find the front wheels mounting a bank at the roadside. Singer's patient fell asleep while dancing. In Singer's case and in one of Fischer's (quoted by Redlich) attacks occurred during coitus.

Aura.

Many patients have a definite aura, a feeling of intense fatigue; in others the attack is said to come on without warning. Some patients can resist the inclination to sleep for times that vary from a few minutes to half an

hour, but try as they will they sleep sooner or later and the longer it is deferred the more sound and the more prolonged is the sleep that almost inevitably follows.

Condition during the attack.

In almost all the published cases the author has seen his patient during an attack. As a rule the statement is made that it resembled exactly normal sleep. In some reports more detail is given from which it is clear that the depths of unconsciousness varies considerably. Briefly the condition in observed attacks was as follows:-

Löwenfeld:	normal sleep, easily awakened.
Stöcker:	true sleep, easily wakened by a call.
Stiefler:	normal sleep, easily wakened, Meyer's reflex present. (This reflex is absent after an epileptic attack.)
Redlich:	normal sleep, easily wakened, slight headache if wakened.
Jolly:	perfectly natural sleep, easily wakened.
Noack:	normal sleep, angry if wakened.
Singer:	normal sleep, sees and hears nothing while asleep, easily wakened.
Mendel:	normal sleep, hears everything, easily wakened, e.g. by raising lids to examine pupils.
Somer:	natural sleep: if he hears conversation he makes irrelevant remarks which he recognises as such and is awakened by his feeling of annoyance.

Goldflam:	appearance of normal sleep, but he sees everything as through a fog and hears everything as through a wall, easily wakened.
Goldflam:	normal sleep, but cannot be awakened, conjunctival reflex present, pupils small reacting to light, eyeballs rolled upwards.
Goldflam:	normal sleep, usually knows what is going on round him but once in prison burning his soles failed to waken him.
Henneberg:	normal sleep, easily wakened as a rule but sometimes needs a good shake.
Gelineau:	normal sleep, the only way to waken him is to shake him violently.

The patient as a rule feels fresh on waking and is wide-awake at once; he knows he has slept and often remembers the content of his dreams.

Tone-loss attacks.

These attacks may be brought on by almost any emotion; hearty laughter is the most potent cause then anger or annoyance. Gelineau's patient at first had his attacks on laughing heartily only but later all sorts of emotions, pleasurable or not brought them on. If when playing cards he found he held a good hand and was likely to win or if in business he saw the prospect of a good deal he felt a sudden weakness, his head fell, the limbs gave way and he sometimes fell asleep. If he had an attack in the street

he walked like a drunken man; when bystanders reproached him he was unable to reply; the more they mocked him the weaker he felt until he fell evading the traffic by a final effort. When a crowd collected "as it does so quickly in Paris" and he heard sympathetic remarks he felt weaker still and recovery was hindered. At the theatre which he visited with great pleasure the thought of enjoying himself caused him to have an attack as soon as he sat down. "His son wakens him if he goes to sleep". As soon as the play begins he follows it with interest and does not have an attack unless he laughs heartily or a sad incident affects him too much. If he becomes enraged he does not sleep while the passion lasts but an outburst is always followed by sleep sooner or later. If he sees two boys fighting and takes the part of one his limbs become flaccid and he is unable to stand." This case is remarkable for the fact that most of the attacks of both kinds were brought on by emotional disturbances.

In one of Somer's cases both kinds of attacks occurred separately but a tone-loss attack was occasionally followed by sleep. For example the patient had a tone-loss attack followed by asleep while he was recounting the painful circumstances in whch his first tone-loss attack occurred.

Condition in the attack.

Descriptions of the condition during the tone-loss attacks are meagre and in most cases are based on hearsay; they are rarely observed by a physician because the patient refuses to laugh heartily in his presence. The statements made on the subject by the various writers are as follows:-

Loewenfeld: If he laughs heartily the muscles go slack and things fall from his hands; he holds on to prevent himself from falling; he grimaces, his jaw falls and he is unable to close his mouth.

Noack: When he is pleased he grimaces and protrudes his tongue; when he laughs heartily he moves his head which falls to one side as if it were loose; the arms hang limply and the legs give way at the knees so that he fears he will fall; things always drop from his hands when he laughs. Anger causes the same symptoms.

Somer: When he laughs his head falls forward, his knees give way and he sinks slowly to the ground unable to move for about half a minute; if called upon to speak he mutters incoherently; he remembers the attack and everything that takes place during it.

Somer: The attacks are caused by hearty laughter and other excitement; he had an attack while dressing - the head sank on the chest, the lids closed, the face was pale, the knees gave way and he sank slowly to the ground, where he remained in a sitting position unable to move for about half a minute; when ordered to speak he stammered but could not

open his mouth properly. Later he recovered his speech, then stood up and finished dressing. He always remembers everything that occurs during the attack; sometimes he is able to repeat words to order during the attack.

Singer: If he laughs he grimaces and his knees give way but he does not fall; he does not lose consciousness.

Henneberg: If he laughs heartily the head falls forward, the jaw drops, the knees give way and he has difficulty in standing; there is no dimming of consciousness.

Jolly: On laughing loudly the head falls forward, the jaw drops, and he has no power in his knees; he is unable to move.

Mendel: He can laugh heartily with impunity but if he is angry the head falls forward and the knees give way.

Redlich: When he laughs the knees give way, he feels as if he will fall and things drop from his hands; he does not lose consciousness.

Stiefler: When angry or annoyed he gets a sudden feeling of helplessness, his knees give way and he is unable to say a word.

Stöcker: Nothing happens when he laughs but if he is suddenly called upon to perform a particular task his strength goes; sometimes if he clenches his teeth and tries hard he can resist the attack and continue working but with diminished strength; the attack lasts less than a minute. When he larks with other boys he loses his strength and the weakest can do what he will with him.

These descriptions are monotonously alike but some of them give details which reveal the important fact that movements occur which cannot be explained by simple loss of tone but are rather of the nature of hyperkinesis, e.g. grimacing, protruding the tongue and stammering. Their importance lies in the fact that they might arouse the suspicion of epilepsy.

In contrast with the sleep attacks which are usually irresistible, patients learn to prevent the tone-loss attacks by refusing to be aroused to hearty laughter. My patient Olive explained this to me clearly and Noack reports that although his orderlies saw many attacks he saw none himself as the patient refused to laugh in his presence. In some patients tone-loss attacks occurred without any emotional cause.

Duration of Disease.

The duration of the disease at the time the cases were published is given below. In several cases this information is omitted from the reports.

Stöcker:	6 months.
Redlich:	6 months.
Loewenfeld:	4 years.
Mendel:	4 years.
Henneberg:	5 years.
Jolly:	6 years.
Noack:	6 years.
Goldflam:	9 years.
Goldflam:	14 years.
Singer:	15 years.
Goldflam:	21 years.

During the time that the disease had persisted its severity was fairly constant and one gets the impression that it persists with slight variations in intensity throughout life.

Effect of Treatment.

Many forms of treatment have been tried without success. Bromides and other antiepileptic remedies produce no favourable effect. Some have tried to diminish sleep during the day by making the night sleep more profound, others have given caffein and other drugs reputed to prevent sleep. Thyroid and various polyglandular preparations have also been used. In many instances the attacks became less frequent while the patients were resting in Hospital but they recurred with the original frequency soon after discharge.

Results of analysis.

Information gained from the study of these cases allows me to modify several statements made by previous writers. The disease is not confined to the male sex. A more characteristic case than that of my patient Olive could not be imagined. Hitherto the only published female cases were those of Nevermann and Kollewijn who wrote on "narcolepsy in pregnancy". In these cases sleep alone occurred - no tone-loss - and the patients became normal

after delivery. Among eleven cases (unpublished) seen by Redlich, two were females.

It is certain, then, that though males are much more often affected than females, this sex may also suffer from the disease.

The average age at onset in the published cases included here was 23½ years. In my own cases the ages were 11, 12, 15, 20 and 35 years.

Redlich states that the ages in his unpublished cases varied from before puberty to beyond the age of forty. In several reports it was stated that the patient had always been sleepy and it may be that the onset is sometimes earlier than my figures indicate. Nevertheless the statement that the disease begins at puberty,(Purves Stewart and others) is certainly incorrect. Onset at puberty has been used as evidence for the view that narcolepsy is due to disorder of the ductless glands; this conclusion may be correct but my figures shew that one of the reasons for it is unsound.

In the foregoing analysis of the attacks in true narcolepsy I have found it convenient to consider the two "kinds" of attack separately. In this I have followed other writers on the disease, but I cannot follow them when they infer that the two kinds of attack are as distinct in nature as they sometimes are on superficial examination; for close scrutiny makes it clear that every gradation occurs between mild tone-loss with no dimming of con-

sciousness whatsoever to profound and prolonged sleep. For purposes of description and for didactic exposition one would be justified in giving the bald facts: two "kinds" of attack occur, sleep attacks without cause, and tone-loss attacks on emotion. In these few words the features that distinguish true narcolepsy are named and anyone possessing this knowledge would be able to recognise a "typical" case. But for our present purpose a more searching enquiry is necessary. It may be that there are cases in which both kinds of attacks always occur quite independently in a pure form; on the one hand sleep attacks without any preceding tone-loss, in which the patient falls into a condition indistinguishable from normal sleep, on the other attacks of pure tone-loss with complete retention of consciousness throughout; but I feel sure that these cases, if they exist, are rare. The "aura" of a sleep attack, the feeling of weakness and intense fatigue that so often precedes the onset of sleep, is an expression of loss of tone in the muscles and where this "aura" is not followed by sleep as it usually is but constitutes the whole attack, it is difficult to place the attack in either group. My patient Olive P. often has attacks of this kind. Without any cause she is overcome by a feeling of weakness and excessive tiredness so that it is difficult to move the limbs. This may or may not pass on to sleep. Stöcker says of his patient "if he clenches his teeth and tries hard he can resist the attack and continue working

but with diminished strength". If he gives way the tone diminishes still further, he is unable to move the limbs and may fall asleep.

Again the depth of unconsciousness varies greatly in the sleep attacks. In many the sleep is so light that it is difficult to decide whether the attack should be classed as a sleep or a tone-loss attack. "Sees and hears everything while asleep," "hears and remembers everything" "he sees everything as through a fog and hears everything as through a wall," "usually knows what is going on around him"- these are some of the statements that occur in descriptions of patients who were said to be in attacks exactly resembling normal sleep. These remarks apply to some of the attacks only; in others in the same patient sleep was moderately deep, so that firm shaking was necessary to waken him, or even profound. In the mildest attacks where the patient hears and remembers everything I suspect that it is the combination of loss of tone and immobility with closure of lids that gives rise to the common statement that his appearance was that of a person in quiet normal sleep. My patient Mrs. C. told me that "they always think I am asleep, my eyes close at the beginning of the attack; I try to open them but cannot; I hear them saying that I am asleep. I try to speak but cannot move my lips or say a single word."

Some of the attacks, then, that have been called sleep attacks are perhaps better described as severe tone-

loss attacks - transitions between tone-loss and sleep. On the other hand while some patients undoubtedly have pure tone-loss without dimming of consciousness, many of the attacks that have been placed under this heading are also transitional. In several cases including one of my own (F.W.) tone-loss attacks on emotion ended in sleep. In some cases tone-loss attacks occurred alone for some time to be followed later by sleep attacks with or without an emotional cause. In Gelineau's patient both kinds of attack nearly always came on with pleasurable emotion - not at other times. One of Goldflam's patients had both kinds of attack, the tone-loss attacks being sometimes connected with emotion and sometimes not.

These facts lead to the following conclusions: in typical cases two kinds of attack occur, sleep without cause, tone-loss on emotion; but many attacks are transitional and do not fall readily into either category. Although sleep usually comes on without cause it may follow tone-loss brought on by emotion. Although tone-loss usually follows an emotional disturbance it may come on without cause. Hence the underlying mechanism is the same in all the attacks. Essentially they are expressions of the same process differing only in degree. What this process is I shall consider later.

In three cases that I accept as examples of true narcolepsy sleep attacks alone are described. Tone-loss

attacks often follow sleep attacks after a considerable interval, and it may be that in my case (L.W.) where the duration of the disease is short they may appear later. In the other two the long duration of typical sleep attacks without the appearance of any other disease to which they may be attributed causes me to accept them and admit that sleep attacks alone may occur in genuine cases.

Differential Diagnosis.

To one unacquainted with the manifestations of true narcolepsy a description of the symptoms by a patient or his friends would certainly suggest epilepsy. "He grimaces, the head falls forward, the limbs become slack and he sinks to the ground," might well be an account of a mild epileptic seizure. Moreover epileptics often sleep after an attack and as it is perhaps true that irresistible sleep is occasionally an epileptic equivalent, the statement that the patient fell asleep at odd times would not divert the uninitiated physician from his false diagnosis. But to one familiar with both diseases confusion is hardly possible. Even if we admit that sudden attacks of apparently normal sleep occur in epilepsy, it cannot rightfully be maintained that these attacks may be the only manifestation of epilepsy throughout long years - unless we alter our definition of epilepsy.

It has happened in several cases that tone-loss attacks occurred alone for a few months before the sleep

attacks began. In these cases the diagnosis of epilepsy would only be made if the history were taken carelessly for a most important feature of idiopathic epilepsy is that the attacks come on without apparent cause whereas in narcolepsy the tone-loss attacks are "reactive", i.e. there is a definite exciting cause, namely emotion.

In epilepsy the disease soon assumes a severe form in young patients with frequent minor seizures who do not respond favourably to appropriate remedies; in narcolepsy the attacks are often very frequent, antiepileptic remedies have no effect upon them and the attacks go on with unaltered severity for years: in epilepsy mental deterioration and psychical defects are characteristic sequels that appear soonest in its victims who have frequent abortive seizures; narcolepsy, in spite of its long duration and the frequency of its attacks, does not impede mental development nor give rise to psychical defects: in epilepsy the first major attack is rarely delayed more than a few years; patients with narcolepsy have been observed for such periods as 14, 15 and 21 years; in none of the cases was there ever a convulsive attack of any kind; in no case was there a family history of epilepsy. These - I need not mention others - are differences which cannot be ignored. I have perhaps laboured this point somewhat but there is some justification becuase many authorities e.g., Oppenheim, Bleuler,

Dejerine, Kraepelin, and Bregman still think that "some of the cases (of narcolepsy) are hysterical some epileptic" and do not accept narcolepsy as a disease sui generis. My own mind is quite clear on the matter; narcolepsy and idiopathic epilepsy are not the same because in narcolepsy the tone-loss attacks are almost always reactive, in genuine epilepsy the attacks are never reactive: this feature alone is sufficient to shew that the two conditions are fundamentally distinct.

Pyknolepsy.

I have defined pyknolepsy elsewhere as "a disease with an explosive onset between the ages of four and twelve years, of short, very slight, monontonous epileptiform seizures of uniform severity which persist for weeks, months or years uninfluenced by anti-epileptic remedies, without impeding normal mental and physical development and ultimately cease spontaneously, never to recur". In this disease which is peculiar to children the attacks consist of an inhibition of the higher psychical processes lasting from five to ten seconds; the power of speech and of voluntary movement is in abeyance but automatic movements are retained; the child stands with the limbs relaxed staring vacantly, the lids may flicker, the eyeballs may roll upwards, but there are no convulsive movements and consciousness is never entirely lost. I have seen many

of these attacks. They are indistinguishable from petit mal; they do not resemble normal sleep and there is never any "chute ou astasie", no dropping of objects, no sinking to the ground as in narcolepsy.

It is unfortunate that Friedmann who first described this disease used the expression "short narcoleptic attacks" for this has caused great confusion among German writers, many of whom still agree with Friedmann that the short attacks in pyknolepsy are of the same nature as the sleep attacks in narcolepsy and describe the two diseases under one heading.

Pyknolepsy begins between the ages of four and twelve years and terminates spontaneously in a few months or years; narcolepsy rarely, if ever, begins before puberty and may persist throughout life: the attacks in pyknolepsy in no wise resemble sleep; they last a few seconds only; one kind of attack alone occurs and it comes on without cause, never as a result of emotional disturbance. Except that attacks occur in both diseases, there is, so far as I can see, but little similarity between them. Certainly the differences justify a distinctive name for each.

Hysteria.

For those to whom "hysteria" and "functional nervous disorder" are more or less synonymous terms the symptoms in narcolepsy may be hysterical, but if "hysteria is a

pathological state manifested by disorders which it is possible to reproduce exactly by suggestion in certain subjects and can be made to disappear by the influence of persuasion alone" (Babinski) then there is certainly no connection between them, for suggestion plays no part in narcolepsy and counter-suggestion has been tried without avail. There is never anything hysterical in the ordinary sense in the psychological make-up of patients with narcolepsy, they never suffer from the recognised manifestations of hysteria, and I am quite unable to agree with those who consider that "most of the cases are hysterical, some epileptic."

Lachschlag.

In this condition, first described by Oppenheim, patients fall unconscious on laughing heartily. I have seen one patient only with this symptom. In my patient, as in Oppenheim's, no other kind of attack occurred, in particular no sleep attacks. I have not made a special study of these cases, but so far as I know the patient always loses consciousness and sleep attacks never occur. For these two reasons I think that Lachschlag should be looked upon as distinct from narcolepsy.

Other conditions in which excessive or untimely sleep occurs

Narcolepsy has been described in a number of un-

related conditions. Fat people, as in the classical case of the Fat Boy in Pickwick, are inclined to drop off at odd times. Obese patients with pituitary disease are often somnolent. One of my patients frequently fell asleep for a few seconds while she was under examination. Dercum wrote a paper on "profound somnolence or narcolepsy" in a patient with pituitary disease and many others have referred to the frequency of somnolence in these cases. I know of two papers in which the tendency to sleep during the day, after an attack of encephalitis lethargica was described as "narcolepsy after encephalitis lethargica", and I have seen the name narcolepsy applied to the prolonged sleepy state that occurs in the early stages of this disease. Many patients with cerebral tumour are somnolent; some have what one of my patients called "dog-naps" during the day and the tendency to sleep at odd times is often very noticeable. But in none of these conditions, nor in any of the many cerebral and general acute and chronic diseases in which patients are drowsy should the word narcolepsy be used if it is to retain any value. In the conditions mentioned and in others where excessive or untimely sleep occurs the patient presents some evidence of the disease of which sleepiness is a symptom, whereas true narcolepsy occurs in persons who are otherwise healthy. In true narcolepsy characteristic attacks occur on emotion. This <u>never</u> happens in diseases where sleep attacks are a symptom of some other disease.

Nomenclature.

For various reasons a number of names have been suggested to replace the original name that Gelineau applied to his case.

Singer objects to narcolepsy because, like narcosis, it suggests artificial sleep; he proposes the name hypnolepsy in its stead.

Henneberg thinks the attacks should be labelled ekleiptic or ekplectic.

Curschmann and Prange agree with Walther that the name narcolepsy should be abandoned because it suggests some connection with epilepsy. Their suggestion is Einschlafsucht, but we have "sleeping sickness" and "sleepy sickness" already - and an English translation of their name would create further confusion. One objection to narcolepsy is that Friedmann called the attacks he described in children "short narcoleptic attacks". To show how readily we confuse a name for a thing - this has led one writer to classify Gelineau's disease and Friedmann's disease which are absolutely distinct, as narcolepsy types i. and ii. For English writers at least this difficulty will not arise because the name pyknolepsy which I chose for Friedmann's disease is gradually being adopted in this country. It is used in the most recent edition of Osler's textbook and will be used in the edition of Price's text-book which is now in the press.

It is unfortunate that narcolepsy is used now for a symptom common to many dissimilar conditions; this is perhaps a good reason why a new name should be invented to designate a new disease sui generis; but I am strongly in favour of retaining the name narcolepsy for Gelineau's disease. Confusion would be avoided I think, if we distinguished between true idiopathic narcolepsy and symptomatic narcolepsy. The name narcolepsy when used without qualification should mean true idiopathic narcolepsy; when it refers to somnolence or short attacks of sleep as a symptom of some other disease it should be described as symptomatic narcolepsy.

The nature of the symptoms.

Hitherto I have written of "sleep attacks" taking it for granted that the condition of the patient in them was that of a person in normal sleep. I have done this because I am convinced that it is true, but it is right to mention that this opinion, though held by most writers on the subject, has not gained universal acceptance. Wendoverić in a recent paper states that the sleep attacks in narcolepsy are characterised by the occurrence of "grelle Träume" but this is certainly by no means constant or even frequent in narcolepsy and vivid dreams are common enough in normal sleep. The fact that patients with narcolepsy sometimes sleep while walking, riding and so on is of little importance. Anyone with War experience

knows that a tired man can walk or ride in a semi-sleeping state which would soon pass on to normal sleep if the conditions were favourable: anyone who has closely questioned patients who complain of sleeplessness must be familiar with states transitional to sound normal sleep in which passing events are more or less appreciated and capable of recall. Goldflam has given particular attention to this point and after careful observation of one of his patients he was able to state that the condition during the attacks was in every ascertainable way exactly that of normal sleep.

Patients with narcolepsy, then, have sudden attacks in which they fall asleep: here we are dealing not with any qualitative change in the reaction of a human being to his surroundings, but merely with an exaggeration of events that occur in the state we call normal. A man who falls asleep on a warm afternoon after a good lunch or one who sleeps during a dull discourse is not held to be suffering from disease. Individuals vary greatly in this respect. One of the most active of my colleagues drops off to sleep, just as a dog does, when he is sitting alone with nothing better to do. But patients with narcolepsy sleep not only under circumstances that invite sleep but also under the most diverse conditions: once the inclination is felt sleep is usually inevitable although it may endanger life. More than one case of narcolepsy

was detected during the War when a man under arrest and liable to be shot for sleeping at his post was submitted for medical examination prior to his court martial. In narcolepsy sleep is often brought on by hearty laughter .

In these respects our patients so far overstep the arbitrary limits of the normal that we are justified in saying that they suffer from disease.

I have said that there is very little difference of opinion regarding the unity of the sleep attacks and normal sleep. Concerning tone-loss attacks opinions are still sharply divided. The expressions "helpless with laughter" "laugh - I nearly died!" "speechless with rage" and many others, remind us of the normal effects of emotion. That one of the patients I have described lost all his strength when larking with his mates so that the weakest could overpower him would not surprise a normalperson who is ticklish. That another felt weak when called upon to perform a certain task would be understood by any one who has ever suffered from ordinary stage fright or gone "over the top". Many must have experienced the effect of a sudden call for quick judgment when faced by imminent danger when motoring and the curious feeling that pervades the body for the instant that elapses between thought and appropriate action. I once sat beside a driver who was so overcome by the sight of approaching danger, which he had ample time to avoid, that

he sat helpless while I braced myself for the serious collision that followed. I suspect that many motoring accidents result from similar tone-loss attacks. The rabbit or bird "fascinated" by the snake is perhaps in the same condition, likewise the animals that sham death in the face of danger.

Curschmann and Prange in agreement with Schuster enumerate many of the well-known effects of emotion on the musculature of man and lower animals and protest vigorously against the acceptance of tone-loss as characteristic of narcolepsy. "We must emphasise very strongly" they say, "that we see in affective hypotonia nothing characteristic of narcolepsy but merely a widespread form of motor reaction to emotion that occurs in normal people."

These words from one (Curschmann) whose writings I have often admired fill me with astonishment. The effects of emotion on normal persons are familiar to all, but though uncontrolled laughter reduces many to a state of helplessness, this only occurs when they have more or less voluntarily "let themselves go" and we do not see people otherwise healthy in mind and body sink helpless to the ground unable to move for half a minute or more, <u>every time</u> they laugh with ordinary heartiness, nor do they <u>ever</u> fall asleep at these times as patients with narcolepsy often do.

Normal people do not fall asleep when they see the prospect of good business or hold a good hand at cards, or study a stroke at billiards, or feel sad or gay at the theatre - it is not necessary to multiply examples. A perusal of the cases that have been published should convince anyone that the effects of emotion on patients with narcolepsy though undoubtedly alike in nature to those in normal persons so far differ from them in degree that they must be looked upon as pathological.

To my mind tone-loss in narcolepsy is as characteristic of the disease as the sleep attacks themselves. Given a case with sleep attacks alone the diagnosis is difficult for sleep attacks indistinguishable from those of true narcolepsy occur as a symptom in many dissimilar diseases; but if definite tone-loss attacks are present as well the diagnosis is made certain for the combination is seen in no other condition whatsoever. My conclusions concerning the nature of the symptoms are: the sleep attacks are attacks of normal sleep; the tone-loss attacks are certainly characteristic of the disease.

Pathogenesis.

As the symptoms in narcolepsy are exaggerations of normal phenomena it is clear than an understanding of them will come with further knowledge of the physiology of sleep and of the effects of emotion. On these points

our knowledge is, to say the least of it, incomplete. Gelineau thought sleep occurred in narcolepsy because the supply of oxygen to the pons was insufficient. Löewenfeld spoke of over-excitability of the vasomotor apparatus and more recently Somer and Oppenheim have written of pathological liability of vasomotor centres. Friedmann attributes the attacks to an abnormal fatigueability of the brain. Henneberg expresses himself as follows: "die Vorstellung liegt nahe dass bei der Narkolepsie - neurose im Zentralnerven-system eine abnorme Disposition für das Eintreten von Hemmung auf psychischem und motorischem Gebiet besteht; Diese ist eine eigenartige und unterscheidet sich wesentlich von der abnormen Ermüdbarkeit asthenischer und erschöpfter Individuen". I give this quotation because of the use of the word inhibition and because though unsupported by experimental evidence at the time Henneberg wrote it, it contains the germ of what I hope to show is the truth.

Kahler looks upon narcolepsy as an abnormal fatigueability of the brain whose cause is "eine auf konstitutioneller Basis beruhende narkoleptische Reaktion" - hardly a helpful explanation.

Redlich - who is, if I may say so with propriety, the only writer beside myself who has made a serious study of the disease - has made some interesting observations without committing himself to any definite theory. Following Mauthner and Economo who have postulated "sleep centres" in

the grey matter of the mid-brain Redlich suggests that the mechanism for the sleep attacks in narcolepsy is also situated in this region. In this neighbourhood too are structures which seem to be closely connected with muscle tone and emotion. The curious response to stimuli that occurs in the so-called "thalamic syndrome" is familiar to every neurologist. A number of writers connect the thalamus with the motor expressions of emotion. The mimetic facial paralysis in thalamic lesions is a good example, and forced laughter and forced weeping have also been cited, not with justice, I think, in this connection. Although the evidence is not beyond criticism, I think the view may be accepted that the interplay of strong emotion and its motor, vasomotor and vegetative expressions is certainly modified by lesions in subcortical centres, particularly in the optic thalamus, and that part of the mechanism for these reactions in normal individuals is situated in this region.

Further, although it is certain that many unjustifiable statements have been made about the functions of the basal ganglia, it cannot be denied that disturbances in the amount and distribution

of muscle tone occur in many diseases where these structures are diseased. In paralysis agitans negative lesions in these parts allow a constant general increase in tone. In narcolepsy, it may be, a positive lesion, a peculiar response to a sudden emotional disturbance, produces sudden general loss of tone.

These facts suggest that the parts of the brain that behave abnormally in narcolepsy are the "centres" connected with sleep and muscle tone in the basal ganglia. I shall discuss the pathogenesis of the disease further when I have considered the nature of normal sleep, but before I do this I must say something about the possible relationship between narcolepsy and the ductless glands.

Here again nothing definite can be stated. I can only indicate the points of contact. In several cases of narcolepsy, including one of my own, the sella turcica was remarkably small; but little value can be attached to this as the sella is very small in many persons who appear to be perfectly healthy. Fat people are apt to drop off to sleep at odd times; obesity is common in pituitary

disorder. Patients with gross pituitary lesions, for example tumour, often have sleep attacks exactly like the "dog-naps" in narcolepsy. A patient of my own fell asleep several times during her examination and many cases of "narcolepsy in pituitary disease" have been published. But considering the very large number of patients we see with pituitary and other ductless gland disorders the occurrence of pathological sleep is relatively rare, and patients with pituitary disease never, so far as I am aware, have the tone-loss attacks of true narcolepsy. It is perhaps significant however, that the region that contains "centres" for tone and sleep - the infundibulum and its surroundings - also contains important vegetative "centres" and nervous connections with internal secretory organs, especially the pituitary body: reversely it is probable that the activities of this region can be influenced by the ductless glands. The subject is far from clear but it seems reasonable to suggest that disturbances in internal secretion <u>may</u> play some part in the pathogenesis of true narcolepsy.

The Mechanism of Normal Sleep.

Of the nature of sleep little is known although the sleep problem has always interested physicians and philosophers and surmises concerning it are numerous. The most important hypotheses are discussed by Trömner in his book "Das Problem des Schlafes" (1912)., and by Pieron in his book "Du Sommeil" (1913). I shall not burden my thesis with an enumeration of the many "theories" of sleep mentioned by these writers - Pieron gives some 15 groups of theories - but shall begin where they left off. Trömner considered existing theories only to condemn them and formulated an hypothesis based on the assumption of the existence of a "sleep centre" in the optic thalamus. But isolated lesions in the thalamus, so far as I know, have never given rise to excessive sleep. The only case I have encountered that bears on this point is one of Hirsch's where "an abscess as big as a hen's egg" was found in a patient who towards the end of his illness had slept excessively. But the fact that this symptom was of late onset in a case where the abscess must have been present a long time might well be used as evidence against Trömner's contention. Among the hypotheses rejected by Trömner is that of Mauthner who placed the hypothetical sleep centre in the periaqueductal grey matter. In the light of knowledge gained from a study of the lesions in epidemic encephalitis (encephalitis lethargica), this view becomes important and demands consideration.

In 1890 Mauthner took part in a discussion in Vienna on "a curious and deadly sleeping sickness" then called Nona, and foretold that the lesions causing sleep in this disease would be found in the grey matter surrounding the aqueduct of Sylvius. He had never seen a case of Nona but based his prediction on his special knowledge, as an ophthalmologist, of the ocular symptoms and the site of the lesion in a number of pathologicalconditions in which excessive sleep and ocular palsies are associated, e.g. in Wernicke's acute anterior polioencephalitis. Time has provided much evidence in favour of Mauthner's view and, without prejudice to what I shall say later concerning the mechanism of normal sleep, it is certain that pathological states, at least resembling sleep, are often associated with lesions in the areas he mentions. In particular numerous careful pathological studies in epidemic encephalitis have shown that one of the sites of predilection for the inflammatory lesions in this disease is the grey matter around the third ventricle, around the aqueduct of Sylvius and in the floor of the 4th ventricle.

These findings have led Economo to place the most important part of the nervous apparatus concerned in normal sleep in the posterior wall of the third ventricle and in the adjoining grey matter in the interpeduncular region."

The conclusion that lesions in this part of the brain can produce disturbances of sleep can hardly be gainsaid in

face of the volume of evidence supplied in the findings in encephalitis lethargica; but one criticism can be made; the lesions in this disease are diffuse and never sharply confined to the sites of predilection. Economo accepts this restriction and awaits confirmation of his view from the examination of cases with a lesion confined to these parts. Brissand's famous case of a solitary tubercle in the substantia nigra proved that a lesion here can produce the symptoms of paralysis agitans and led us to look there with complete success for the constant lesion in the Parkinsonian syndrome after encephalitis lethargica. Have isolated lesions of the periaqueductal grey matter been observed, and if so, did they produce pathological sleep? I know of two cases that almost fulfil Economo's requirements. In one (Luksch) a man with infective endocarditis slept almost continuously during the fortnight before his death; an embolic abscess was found "in the grey matter of the caudal part of the third ventricle and in the wall and surrounding parts of the beginning of the aqueduct."

Pette recorded a case where a man lay for three months from the acute onset of his illness to his death in a state which "resembled in a remarkable manner the lethargic condition seen in encephalitis lethargica so that the possibility of the presence of this disease was considered to be highly probable." After death an area of softening was found "in

the tegmentum between the substantia nigra and the aqueduct." Pette concludes "that there exists in the grey matter in the floor of the third ventricle a point which has an important connection with the function of sleep; probably it is the sleep centre itself."

These cases are of considerable importance for they suggest that lesions in this part account for the disorders of sleep in encephalitis lethargica. But though they may account for them they do not by any means prove the existence of "sleep centres" in this region. I shall return to a consideration of Mauthner's theory later when I attempt to reconcile this theory with the view I shall set forth that sleep is a function of the cerebral cortex.

In Pieron's book I found much to interest me. This writer concludes his critical analysis of the more important theories of sleep with the following words: "en somme, parmi les théories il on est qui sont nettement contredites par les faits, théories anémiques, histologiques, osmitiques, théories des sécrétions internes, d'autonarcose carboniques, théories toxiques invoquant un certain nombre de substances définies. Il en est dont on peut dire qu'elles ne sont pas suffisament expliquatives, comme la théorie de l'epuisement, ou qu'elles restent purement hypothetiques comme la théorie de l'inhibition, complété ou non pas la conception d'un mechanisme protecteur. Est-il alors possible

d'edifier une théorie toxique qui soit plainement satisfaisante? C'est la le probleme que nous allons avoir à discuter."

Pieron described a substance - hypnotoxine - which he obtained from the blood serum and cerebro-spinal fluid of dogs that had been kept awake for long periods; by injecting a few cubic centimetres of hypnotoxine into the ventricles of healthy dogs he produced a condition resembling sleep and elaborated a theory that sleep results from the action of fatigue products that accumulate during the waking state. This is of course merely a variation of the existing "toxic" theories, but differs from them in that it is supported by evidence gained from experiments. I could not convince myself that the lethargic state in Pieron's dogs was normal sleep; they slept willy-nilly; they could not be kept awake after the injection and once asleep they could not be roused. I find it quite impossible to explain by any purely toxic theory the rapid passage into sleep and the rapid awakening to full consciousness that occurs in normal sleep. Pieron was well aware of the defects of all toxic theories, and to make his own theory "pleinement satisfaisante" he was forced to think of "some kind of inhibitory mechanism" whose existence had never been demonstrated.

"La notion d'inhibition" he says "n'est pas physiologiquement demontrée pour les centres encephaliques supérieurs."

This, as I shall proceed to show, is no longer true, for since Pieron wrote these words Ivan Pavlov has demonstrated the existence of an inhibitory mechanism in the central cortex and has done much to explain the nature of sleep.

This genius has truly said that "when the physiologist begins to study the highest parts of the central nervous system, his methods change; he ceases to observe the reaction of the organism to external stimuli and instead of describing phenomena in terms of physiology introduces psychological ideas derived from his own consciousness". The resulting confusion is great; indeed it is almost impossible for a working neurologist to think clearly about the functions of the highest centres because the counters of thought - the words he must employ - are often of psychological origin and for the most part meaningless. My study of Pavlov's work has shown me that it is possible to correlate changes in the organism, which appear at first sight to be most intricate and beyond the powers of analysis, with external stimuli; further that the phenomena may be investigated by physiological methods and the results expressed in purely physiological terms. I am tempted to enlarge on the significance of Pavlov's remarkable work but I must confine myself to that part of it which has a direct bearing on my thesis.

For the development of my argument it is necessary to

refer very briefly to "conditioned reflexes".

In studying the activities of the highest cerebral centres we can distinguish reflex activities with nervous connections present at birth and associated reflexes which appear during life. If indifferent stimuli of any kind frequently accompany a stimulus which evokes an inborn reflex, these stimuli by themselves soon begin to evoke the same inborn reflex by "association". These associations are true acquired reflexes which can be investigated by physiological methods. Pavlov calls the inborn reflexes "unconditioned" and the acquired reflexes "conditioned". From the moment of birth paths for conditioned reflexes are constantly being laid down; but the response to conditioned stimuli is not inevitable for if it would be untimely or out of touch with reality it may be inhibited. The following examples will explain my meaning.

If an indifferent stimulus, say a certain sound, regularly precedes food by a certain interval, this sound soon begins to evoke the normal response to the presence of food in the mouth - the secretion of saliva. If after the conditioned reflex is firmly established the stimulus is given but food is withheld the sound gradually loses its effect on repetition until no response is obtained, i.e., the reflex is inhibited. This inhibition disappears spontaneously after a time if the animal is left alone and the conditioned res-

ponse will be obtained again, say next day. This phenomenon for which no name exists in English may be called temporary suppression, or eclipse, of the conditioned reflex. (The German word which Pavlov used is Erlöschen but this means obliteration, to be extinguished, to go out, to die out, to expire, suggesting permanent obliteration. A word is required which makes it clear that the reflex is not abolished but merely temporarily suppressed).

Again, in an instance where food regularly follows the sound in five seconds, and the conditioned response begins at the third second; if the procedure is altered and food follows after an interval of three minutes, at first the conditioned reflex disappears quickly; on repetition of the sound it reappears but only during the third minute. In the earlier stage the stimulus loses its effect and the last part only is active. This is also an inhibition. I shall refer to it as delay of the conditioned reflex, or more briefly as delay.

If another stimulus, say mechanical stimulation of the skin is combined with an effective conditioned stimulus (e.g. a sound) and the animal receives no food after a combined stimulus, then in this combination the sound loses its effect but still retains it when it is given alone. This is also an inhibition. I shall call it conditioned inhibition.

Finally if mechanical stimulation of a point on the skin is made an efficient conditioned stimulus, then similar stimulation of the surrounding parts will also evoke the reflex; the nearer the original point the more powerful the response. If now on repetition food is always given after stimulation of the original point but never after stimulation of neighbouring parts the latter gradually lose thier power to excite. This I shall call differential inhibition.

These different forms of inhibition - eclipse, delay, conditioned and differential - are grouped together as internal inhibition. In passing I cannot resist the temptation to refer to the apparent complexity of these reactions, especially differential inhibition. They are the same as those complicated reactions, in performing animals for example, which seem to be expressions of high intelligence and considerable reasoning power. But they are matters of reflex and inhibition; they can be weighed and measured; they obey rigid physiological laws.

I must now consider the relation of internal inhibition to sleep and give evidence for the belief that sleep and internal inhibition are subserved by the same mechanism.

From the beginning of his researches on conditioned reflexes, Pavlov was greatly hindered by somnolence and sleep which overcame his animals during the experiments. Animals chosen specially for their liveliness and wakeful-

ness when free, succumbed readily and sleep often terminated the experiment before the observation was complete.

It would happen , for example, after a good conditioned reflex had been established, that the animal became somnolent or fell asleep during the time that the conditioned stimulus was active. Sleep was often so profound that firm prodding was required to dispel it from an active and greedy animal that had not been fed for 24 hours. In one instance a good conditioned reflex had been established; food followed the stimulus in ten seconds and the animal gave a very active secretory and motor response during the ten seconds between stimulus and food; but when food was withheld for 60 seconds a remarkable change occurred; the dog became sleepy during the waiting period, the conditioned response disappeared, and the dog that had never slept in the experimental stall before, fell asleep every time the stimulus was repeated.

The same tendency to sleep was seen during another series of experiments in which conditioned reflexes were not used. When a new indifferent stimulus is given to an animal it responds by placing its receptors in the best attitude for receiving the impression; it looks towards a light, it cocks its ears in the direction of a sound, and so on. Pavlov calls this reaction the orientation reflex. If such a stimulus is repeated at frequent in-

tervals the reflex diminishes steadily until it disappears and if fresh dissimilar stimuli are not given the animal becomes somnolent or falls asleep. If this test is repeated several times with the same stimulus the animal can be made to sleep with absolute certainty. Special investigations by one of Pavlov's pupils have shown that this gradual failure to react to the repetiton of a single stimulus follows the laws governing eclipse of a conditioned reflex and it is almost certain that the mechanism is the same in both phenomena.

These and many similar experiences convinced Pavlov that the sleep that obtruded itself so persistently was something more than an annoying complication in his experiments, and in the end the problem of sleep itself engaged his particular attention.

After testing and considering various hypotheses during the course of ten years steady work, he finally reached the conclusion that sleep and the internal inhibition that he had described in his work on the conditioned reflexes were one and the same process. "With this conclusion" he says "everything agrees that we have learnt during twenty years work on conditioned reflexes", and special researches based on this conclusion have served to confirm it.

The main factor involved in this hypothesis is that

every more or less prolonged stimulus to the cortex, whatever its nature and however strong it may be,if it is not accompanied by stimuli to other parts or if it is not displaced by other stimuli, leads inevitably to somnolence and sleep. The conditioned reflex, even when it concerns the most potent of all stimuli - food, leads to sleep if it plays on an isolated spot on the cortex without being displaced by the mass stimuli that accompany the act of taking food. The same holds true even when the conditioned reflex that calls forth the feeding reaction is aroused by a very powerful electrical stimulus. That monotonous stimuli produce somnolence is of course well known, but before Pavlov illuminated this field it had not been made the subject of scientific research.

I have already given an example of sleep with delay of inhibition. Without going into detail I can say that sleep also occurs during experiments on obliteration and on conditioned and differential inhibitions. Further it is possible to observe the transition of inhibition into sleep and the reverse, the replacement of inhibition by sleep and the summation of sleep and inhibition. As these phenomena supply convincing proof of the essential sameness of inhibition and sleep, I shall give a few illustrative examples.

Food is given to a dog thirty seconds after the conditioned stimulus; the secretion of saliva begins from

five to ten seconds after the conditioned stimulus begins; the experiment is repeated for days, weeks and months, food always being given after the same interval. In the course of time the latent period of the conditioned reflex gradually increases to 15, 20 or 25 seconds until it reaches to within a second or two of 30 seconds, finally no effect is obtained and at this point the animal becomes motionless or falls asleep. In this instance inhibition has passed into sleep. The reverse result is seen in a dog where a delayed inhibition is worked out with an interval of three minutes between the conditioned and unconditioned stimuli, the first part of the interval being active and the latter part inactive. In experimenting upon such an animal it may happen that at first it becomes sleepy as soon as the conditioned stimulus is given, only the last part of the interval being active. On repetition the active period gradually increases while the sleepy period diminishes pari passu until at last sleep gradually disappears. Here sleep has gradually given way to pure inhibition.

The same change from inhibition to sleep has been observed during observations on the orientation reflex. It has been observed during the investigation of delay, where the unconditioned stimulus follows in 30 seconds, that an animal, previously wakeful, falls asleep as soon as the conditioned stimulus is given and remains asleep for 25

seconds, when it wakes and gives a strong reaction. It is obvious that in this case sleep has replaced inhibition and behaves in regard to onset and ending in exactly the same way as pure inhibition. In other cases it was equally clear that a summation of sleep and inhibition had occurred. All these facts enforce the conviction that internal inhibition and sleep are one and the same process.

At first sight this may seem strange for internal inhibition occurs in the wakeful state; it is an expression of activity of the cortex and shows the finest adaptation to stimuli from without, whereas sleep is essentially a condition of inactivity and rest for the cortex. But this difficulty is easily overcome if we look upon inhibition as a partial and strictly localised sleep confined within narrow limits by an opposing process of stimulation, while sleep is inhibition which has spread throughout the cerebral hemisphere and to lower centres in the midbrain.

Guided by this explanation it is easy to understand the cases I have just described; sometimes inhibition spreads widely and the dog sleeps, sometimes it is diminished and sleep disappears. In the case, for example, where sleep was gradually replaced by pure inhibition, it is clear that the process of excitation gradually narrowed the areas under inhibition until sleep disappeared; in other words a condition of equilibrium was attained which

corresponded to reality.

From this we see that if we wish to limit inhibition and prevent it from passing into sleep, or if we wish to displace sleep by pure inhibition, we must produce new points of excitation in the cortex which will counteract inhibition and check its spread. In practice this succeeds admirably. In experimental work where sleep begins to interfere with the tests new conditioned reflexes are worked out with stronger stimuli so that sleep is abolished and the original reflex which had become feeble is restored to full strength. In every-day life we constantly apply the same method to ourselves when we become sleepy. We abolish inhibition by building a new point of excitation in the cortex. We do not express it in these words, however; we are more likely to say "I had to pinch myself to keep awake".

The foregoing brief account of Pavlov's work gives an inadequate idea of the enormous number of facts that he has recorded which confirm his main thesis; sleep is internal inhibition. In this brilliant conception I see a vivid and beautiful illustration of the principle of economy; for if sleep and inhibition are the same, then the mechanism that subserves the highest manifestations of life and renders possible the minute adjustments and endless adaptations of the organism to external changes is based

upon a state of inactivity of the most precious elements of the body - the nerve cells of the cerebral cortex.

This mechanism for internal inhibition that Pavlov has described is situated in the cerebral cortex, for in animals from whom the cortex has been removed none of these results can be obtained. This does not prove that normal sleep is a function of the cortex, but I am convinced that it is so. The more I have thought about the matter during the past few months, the more firm my feeling of conviction has become, and yet I find the greatest difficulty in setting forth the reasons for my belief. It will be granted, I think, that the purpose of sleep is to provide rest; the part of the body for which rest seems to be essential is the Central Nervous System; the part of the central nervous system which requires it most is surely the cerebral cortex. Reason dictates that in this matter the structure that requires rest must provide for itself; I find it impossible to believe that ancient hardy structures like the basal ganglia are likely to show altruistic tendencies and develop "centres" whose function is to protect the cortex.

In the light of Pavlov's work all the facts of normal sleep are readily explained on the assumption that it is a function of the cortex. We know that repeated monotonous stimuli favour sleep; we know that a new stimulus will

waken us when we are feeling sleepy. At every moment during the waking state the cortex is receiving innumerable stimuli of many kinds which may or may not evoke certain reactions; the vast majority of these reactions are purely reflex; they are associated reflexes acquired during life; we react to the stimuli according to the meaning we have learned to attach to them during life - they are conditioned reflexes. But we do not react at once to every stimulus we receive; by inhibition the reaction may be delayed or suppressed. Every time a reflex is delayed or suppressed an inhibitory mechanism is set in motion which is really sleep in a limited area of the cortex; once started this process tends to spread and if unchecked it will extend throughout the cortex and produce sleep; but in the waking state bounds are set to the spread of inhibition by the constant arrival of fresh dissimilar excitations.

One cannot imagine that adaptations so fine as those seen in conditioned and differential inhibition could take place anywhere but in the cortex. In Pavlov's experiments these were also complicated by sleep. The mechanism for internal inhibition is certainly in the cortex; but sleep may pass into inhibition or inhibition into sleep; sleep may be replaced by inhibition or there may be a summation of sleep and inhibition. The two things are so

closely bound up the one with the other that it seems unreasonable to deny that they are one and the same process; if they are, then the mechanism for sleep too must be in the cortex.

How inhibition spreads we do not know; we do not know the ultimate physiology of inhibition itself. A feature of the process that has arrested my attention is this; we have seen that sleep may be produced in dogs by the repetition of a single stimulus; the repeated stimulus exhausts a few cells in the cortex; the animal ceases to respond to the stimulus - a small part of the cortex is asleep. But, this is the curious thing, this sleep is not confined to the exhausted cells but may spread throughout the cortex. It would seem as if prolonged action produced some special substance or evoked some process which prevents further activity in the nerve cells, so protecting them from dangerous exhaustion and that this substance or process can affect surrounding cells which have done no work at all. Pavlov refers to this as "a dark point in the process," but so far he has not given it special consideration or thrown any light upon it.

The sleep problem is not solved but I think that the solution will come with a better understanding of cortical activity and not from a study of lesions in the basal grey matter.

And yet not only somnolence but true sleep is excessive in patients with lesions in the basal ganglia and especially in and around the periaqueductal grey matter. In many diseases excessive sleep and oculomotor palsies are combined - in Gerlier's vertige paralysant, in Gayet's polioencephalitis superior subacuta hæmorrhagica, in Wernicke's acute anterior polioencephalitis, in encephalitis lethargica and in tumours confined to the region of the third ventricle.

At the bedside the combination of ocular palsies and excessive sleep would lead us to place the lesion in the midbrain without hesitation. These facts seem to support Mauthner's theory of "sleep centres" in subcortical structures. I have already quoted Economo who places the sleep centre in the periaqueductal grey matter because ocular palsies and sleep occur in encephalitis lethargica, and Pette, who reaches the same conclusion, But in every condition where ocular palsies and sleep are associated, although the lesions are most obvious in the grey matter, I suggest that conducting paths in the tegmentum of the midbrain or in the thalamus are also affected. In Wernicke's polioencephalitis superior this is certainly the case; in Pette's case which is supposed to give support to the sleep centre idea the lesion lay "between the substantia nigra and the aqueduct" so that most of thetegmentum was destroyed.

In Luksch's case the lesion was "in the grey matter of the caudal part of the third ventricle and in the wall and surrounding parts of the beginning of the aquduct."

My contention is that no case has ever been described in which a lesion strictly confined to the periaqueductal grey matter has given rise to excessive sleep. Where sleep has occurred other structures are involved and as this narrow portion of the brain stem contains the spinothalamic and bulbothalamic tracts just before they reach their goal in the optic thalamus it is clear that lesions in this part will cut off most of the centripetal impulses and prevent them from reaching the cortex.

Now I have said that inhibitions are constantly arising in the cortex by means of which we react appropriately and adjust ourselves to constant changes in our surroundings; with equal constancy local inhibitions are tending to spread and lead to sleep; if sleep is not to occur fresh stimuli must continue to reach the cortex; excitation limits the spread of inhibition. My explanation, then, for the occurrence of sleep in lesions of the tegmentum of the midbrain and of the basal ganglia is this: in diseases affecting these parts the stream of impulses to the cortex is impeded or, more or precisely, the number of impulses that reaches the cortex is diminished so that local inhibitions become general and produce sleep. There is nothing new in

the statement that the cutting off of centripetal impulses leads to sleep. What I have done is to apply the results obtained by Pavlov and to show how sleep is thus produced.

Raising the sluice gates does not cause the water to flow; lesions in these parts do not cause sleep: they allow it to occur.

My conclusion is that normal sleep is a function of the cerebral cortex. Lesions in the neighbourhood of the oculomotor nuclei are often associated with excessive sleep but I do not believe that "the most important part of the mechanism concerned in normal sleep is situated in the adjoining grey matter in the interpeduncular region," (Economo), or that "sleep centres" exist in this part or elsewhere.

For the existence of a sleep centre I have discovered no satisfactory evidence whatsoever. Pavlov has shown that an adequate mechanism for sleep exists in the cortex. Subcortical structures certainly play an important part in producing somnolence and sleep in various diseases and it is highly probable that these structures play an important part in the mechanism of normal sleep; but this does not prove that sleep is initiated or controlled by these centres in healthy persons.

Conclusions on the Nature of Narcolepsy.

It remains for me to discuss the symptoms of narcolepsy once more, this time in the light of Pavlov's researches. Previous writers have described the attacks as if they were

of two kinds, and no one seems to have had an inkling of their essential sameness which Pavlov's work makes so clear. I have shown already that every gradation occurs between mild tone-loss and profound sleep. In the mildest attacks there is slight diminution of muscular tone only; in more severe attacks the tone-loss is general and profound and tone-loss often passes on to sleep; in the most severe attacks the patients fall straight into sleep of varying depths. It will not be doubted that sudden loss of muscular tone on emotion is due to inhibition; I suggest that sleep in this disease is also due to inhibition; in cases where tone-loss precedes sleep I imagine that the inhibitory process spreads to the cortex from lower centres; in cases where sleep alone occurs a more extensive disturbance affects the cortex directly or indirectly and produces sleep which varies in depth according to the extent of its spread. If the cortex alone is affected sleep may be very light and the patient may be able to maintain the erect posture or even to walk; if the spread occurs throughout the cortex and to lower centres, the muscles lose their tone and the patient falls into ordinary normal sleep.

I am not prepared to make a dogmatic statement on the site of the lesion in true narcolepsy. No case has been examined after death but seeing that the symptoms are exaggerations of normal phenomena it is almost certain that there is no detectable anatomical or histological change: the

disease is due to "functional" disturbances. The evidence I gave in the paragraphs on pathogenesis suggests that the part of the nervous system that reacts abnormally to emotion is the subcortical grey matter - one cannot be more precise - and as this part of the brain also contains the paths for centripetal impulses, I imagine that a spread of the process which causes tone-loss may also allow sleep to occur. But my feeling is that narcolepsy is an expression of a curious type of reaction of the whole Central Nervous System and not due to disorderly function in a small part of it.

I have attempted to explain the mechanism of the attacks in narcolepsy but I have not given any reason why certain individuals suffer from this disease.

Now Pavlov found that the tendency for inhibition to spread and produce sleep was much greater in some animals than in others; lively and curious animals with a labile nervous system slept readily, while quiet easy-going animals rarely slept. By studying the general character of the animal it was possible to foretell whether it would become sleepy or not during the experiments. The explanation for this is that in animals lively when running free, sleep was prevented by the constant displacement of inhibition by new and varied excitations; when they were placed in the experimental stall the stimuli were monotonous, inhibition now spread unimpeded and the animals slept quickly. The quiet animals with a more stable nervous system did not need

so many stimuli to prevent the spread of inhibition and sleep did not occur so readily. Conclusion - the tendency to sleep varies with the general nervous make-up of the individual.

During the bad years in Russia (1919-1920) when the dogs (and Pavlov himself I suspect) were underfed and therefore easily fatigued, sleep was so easily produced during experiments on conditioned reflexes that the experiments had to be abandoned. In several cases of narcolepsy the attacks came on for the first time in persons who were physically exhausted or who had been deprived of adequate sleep for a long time; more significant than this, in almost every case of narcolepsy rest in Hospital produced very definite amelioration or even temporary cure with a return of the symptoms when ordinary life was resumed. Conclusion - inhibition spreads more readily in a fatigued brain.

My final conclusion, therefore, is that true narcolepsy is a functional disorder of the nervous system, probably an undue fatigueability of the nerve cells, in certain otherwise normal individuals with a peculiar type of nervous activity which allows an excessive response to emotional stimuli and favours the spread of local inhibitions.

The part in my suggestions which gives me most satisfaction is that the facts in narcolepsy - a disease of man -

support Pavlov's theory - based on experiments on lower animals "that sleep and inhibition are one and the same process".

One thing that puzzled me greatly before I began to study the symptoms of narcolepsy in the light of Pavlov's work, was the apparent dissimilarity in the factors that favoured the onset of sleep attacks. It was not surprising that they should come on "sitting in front of the fire" "after a heavy meal" " in a warm room" "during the rest hour" "riding in a train" and in similar circumstances; but why, I asked myself, do these patients have attacks "at work in a factory" "cycling" "dancing" and even "during coitus". I now see that the attacks are favoured first by a lack of extraneous stimuli and secondly by monotonous stimuli. Even a painful stimulus such as a powerful electric shock produced sleep in Pavlov's dogs if it was repeated and no extraneous dissimilar stimuli reached the animals' cortex; the receptive point in the cortex became fatigued - it slept, and this spread unchecked to cause general sleep: any monotonous stimulus, then, favours sleep; hence in our patients with narcolepsy monotonous movements favour sleep. Several patients including one of my own fell asleep while cycling; one of my patients slept when he had to do a monotonous task in a factory; perhaps the frequent repetition of the same movements explains the occurrence of sleep while walking, riding and even in the extreme cases where it came on while dancing and during coitus.

Another curious feature of the attacks also becomes comprehensible in the light of Pavlov's work. At first I found it extremely difficult to understand why the patients were quite unable to resist the attacks and yet were almost always wakened with extreme ease. Patients who were overwhelmed by sleep which they could not resist, try as they would, awoke at once "when the lids were raised to examine the pupils" or by a light touch or a gentle call. Sometimes they had succeeded by their own efforts in warding off sleep for several minutes oreven for half an hour, but during this time they were extremely drowsy and had a feeling of extreme fatigue: yet, when wakened from their sleep, however short, they felt fresh and wide-awake at once! Inhibition was dispelled at once and completely by a fresh excitation from without as it was in many of Pavlov's experiments. "Nothing I could do myself would keep me awake but a touch or a call or bumping against something woke me up at once" one of my patients said. When I heard this I thought at once of an experiment of Pavlov's on sleep that was spoiled by the sound of an attendant scraping snow from the doorstep. The experiment had been planned carefully, arrangements had been made to eliminate extraneous stimuli, and the animal was just passing into sleep under the influence of a repeated single stimulus when the unexpected stimulus woke it up at once.

I submit then that many of the hitherto unexplained

features in narcolepsy become comprehensible when correlated with Pavlov's discoveries.

The tendency to sleep when few stimuli reach the cortex or when the stimuli are monotonous, the transition of tone-loss to sleep, the ease with which the patient is wakened by a fresh stimulus from without, the immediate and complete wakefulness of a patient so wakened - all these had their counterparts in Pavlov's dogs.

By drawing attention to these similarities I feel that I am doing something towards explaining the mechanism of the symptoms in narcolepsy; the ultimate how and why must remain inexplicable so long as we are ignorant of the how and why of all functional nervous disorders.

Post scriptum.

A case of Narcolepsy following Encephalitis Lethargica.

This remarkable case came to my notice after my thesis was completed. I insert it at the last moment because it has an important bearing on my conclusion concerning the site of the functional disturbance in idiopathic narcolepsy.

Donald R. now aged 17 years, had an attack of encephalitis lethargica in 1923 with fever, sleeplessness, delirium and jerking of the limbs, followed by double vision, restlessness at night and excessive sleep during the day. He recovered in about three months sufficiently to get up and go about, but never became the same boy again. His features were expressionless, his movements were slow, he became very stout, he was bad-tempered and argumentative and still apt to drop off to sleep during the day.

By the middle of 1924 he had improved in many ways; he was sleeping well at night, he had lost the mask-like face, his vision was normal and he was no longer stout; but from that time he has suffered from attacks that trouble him excessively. In his own words "it is fatal" to sit down or to perform a monotonous task, for if he does so he goes off to sleep at once. He cannot sit down to read a book because he sleeps before he reads a page: He dare not sit down in a bus or tube for fear of passing his destination. At his work in a factory he has permission to leave his bench to

walk about in the fresh air whenever he likes because a monotonous task makes him sleep and rapid movement may avert it. As a rule, however, the sleep comes on sooner or later; "if I delay it by moving about I am just packing it up for the future". At the beginning of an attack the feeling of drowsiness is overwhelming and "nothing I can do my self will keep it from getting worse but a new voice or something outside will wake me up". "I was marching along with the scouts one day when I felt sleepy. I was just going off when a boy said 'have you got a knife, Dennis?' this woke me up at once".

The other attacks are even more troublesome. If he laughs his knees give way and he falls to the ground. "At the scouts' camp the boys used to amuse themselves by making me laugh and then running away leaving me helpless on the ground." "I cannot go to the pictures now because if I am amused my head flops on one side and people look at me instead of the pictures." "If I am excited or angry the same thing happens; my head falls down, it is all floppy and wobbly as if the neck were loose; I should drop a cup of tea from my hands; if I were standing up my knees would give way and would let me down." There is no dimming of consciousness in these attacks and they never lead to sleep.

In other respects the boy is perfectly well physically. He presents none of the common residual ocular and motor signs of encephalitis lethargica. His mother, however, says that

his memory is not very good and that he is not such a "nice" boy as he used to be.

To hear this boy describe the conditions under which his sleep attacks occur and the things that prevented them was like reading a description of some of Pavlov's experiments on sleep. A monotonous task caused sleep, nothing arising from within could prevent sleep, exert himself as he would, but a "new fresh voice" (he used those very words himself) or anything coming from without awoke him at once.

So far as I am aware this case is unique. I have not made a special search for accounts of this sequel to encephalitis lethargica in German journals, but I feel sure it has not been recorded by English writers. It is the only case I know of in which tone-loss attacks as well as sleep attacks have occurred apart from idiopathic narcolepsy.

The account of the acute attack of encephalitis is so clear that there can be no doubt about the diagnosis: before this attack he was perfectly well. He now presents none of the usual sequels except a change of temperament: not the slightest degree of Parkinsonism, no subjective or objective ocular symptoms: nevertheless I think we must regard his present condition as a sequel of encephalitis lethargica. The alternative is to look upon this as a case of idiopathic narcolepsy arising in a boy who happens to have had encephalitis lethargica - a view I cannot support. I think this is a case where an organic lesion is so situated in subcortical structures as to produce the symptoms of true narcolepsy that are

usually due to a functional disturbance in the same structures. According to a general principle that I have found of great value I expect to find for every expression of organic disturbance due to dysfunction in a given set of structures a corresponding syndrome from functional disturbance and vice versa.

Many times I have wondered why the symptoms of narcolepsy - a functional disorder - are never produced by an organic lesion; this case provides evidence in support of my general principle.

S U M M A R Y.

The facts.

In 1880 Gelineau described a case and used the word narcolepsy for the first time.

Thereafter until the present day the word has been applied indiscriminately to excessive or untimely sleep as a symptom in many dissimilar conditions.

I record here five cases that have come under my own observation and fifteen cases observed by others, that conform to Gelineau's description; others not included here have been described.

The narcolepsy of Gelineau is characterised by the occurrence of sudden attacks of sleep or loss of muscle tone in the same person at different times.

Both sexes are affected, males much more often than females.

It begins most frequently in adolescence or early adult life and affects individuals who appear to be healthy in every other respect.

Neither hereditary nor exogenous influences are of aetiological importance.

Sleep usually comes on without cause, tone-loss usually follows emotion; but sleep may follow tone-loss on emotion and tone-loss may come on without apparent

cause. In some patients the two kinds of attack remain distinct but every gradation from slight tone-loss to profound sleep has been observed.

The frequency of the sleep attacks varies in different patients from two or three a day to one every few minutes but is fairly constant in each individual. The duration of the attacks varies from a few seconds to several hours and varies greatly in the same individual, sleep lasting longer when the circumstances are favourable. The depths of the sleep varies from a slight doze in which the patient is dimly aware of his surroundings to profound sleep from which he is wakened with difficulty.

Sleep may occur in any circumstances whatsoever and may endanger life. Usually the attack is inevitable. The condition of the patient during the attack exactly resembles normal sleep.

A tone-loss attack may follow any emotion, pleasurable or the reverse, hearty laughter is the most potent cause; in an attack the patient though unable to speak or move may retain full consciousness or his condition may be transitional from simple tone-loss to sleep.

Rest relieves the symptoms; no other form of treatment has any favourable influence upon them. Patients with narcolepsy have been under observation for periods extending up to 21 years; complete and permanent recovery has not been observed; no patient with the symptoms of

true narcolepsy has become epileptic or shown signs of any organic disease to which they could be attributed.

Pathological sleep occurs in many diseases but the combination of sleep attacks and tone-loss attacks is peculiar to true narcolepsy.

Personal opinions.

Gelineau's narcolepsy is a disease sui generis. It is not very rare; most of the cases are diagnosed as epilepsy, some hysteria.

The disease is of considerable medical, military and medicolegal importance.

The name narcolepsy should be reserved for the disease; it should not be applied to excessive or untimely sleep when this is a symptom of some other disease; confusion would be avoided by using the terms idiopathic and symptomatic narcolepsy.

Other names that have been proposed for the disease have nothing to recommend them; the name narcolepsy should be retained.

The "short narcoleptic attacks" of Friedmann are distinct from the narcolepsy of Gelineau and as they were described later they should bear another name; the name pyknolepsy is suitable for them.

The sleep in narcolepsy is indistinguishable from normal sleep; the attacks on emotion, in spite of contrary opinions, are highly characteristic of the disease; I propose for

them for the use of English writers, the names "tone-loss attacks" or "atonic attacks".

The attacks though apparently different in nature are essentially the same; both kinds result from sudden inhibition.

Normal periodic sleep is a function of the cerebral cortex; the internal inhibition of Pavlov is sleep in a narrow area of the cortex; sleep occurs when inhibition spreads throughout the cortex and to certain subcortical centres.

Lesions in the basal ganglia, in the interpeduncular region and in the tegmentum of the mid-brain may cause pathological sleep indirectly by preventing or impeding or otherwise modifying that constant influx of stimuli to the cortex which is essential to prevent sleep; it is improbable that normal periodic sleep is initiated or primarily controlled by "sleep centres" in these parts.

Pavlov's conception of the mechanism of normal sleep receives confirmation from this study of the symptoms in narcolepsy. Pavlov saw sleep in dogs when inhibition spread unchecked; in narcolepsy every gradation occurs from mild tone-loss - a result of inhibition - to deep sleep.

Narcolepsy is a functional nervous disorder that occurs in individuals with a peculiar type of nervous activity; the obtrusive symptoms are probably a result of disorderly action in the basal ganglia or in adjacent

structures in the interpeduncular region; for these parts contain structures that are concerned in the normal reactions to emotion, in the regulation of muscle tone and in the propagation of centripetal impulses to the cortex.

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